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<110> Daniel Cchen  
Ilya Chumakov

<120> Treatment of CNS Disorders Using D-Amino Acid Oxidase and D-Aspartate Oxidase Antagonists

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Pro Glu Arg Gly Ile Tyr Asn Ser Pro Tyr Ile Ile Pro Gly Thr Gln			
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aca gtt act ctt gga ggc atc ttc cag ttg gga aac tgg agt gaa cta			893
Thr Val Thr Leu Gly Gly Ile Phe Gln Ile Gly Asn Trp Ser Glu Leu			
235	240	245	250
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Asn Asn Ile Gln Asp His Asn Thr Ile Trp Glu Gly Cys Cys Arg Leu			
255	260	265	
gag ccc aca ctg aag aat gca aga att att ggt gaa cga act ggc ttc			989
Glu Pro Thr Leu Lys Asn Ala Arg Ile Ile Gly Glu Arg Thr Gly Phe			
270	275	280	
cgg cca gta cgc ccc cag att cgg cta gaa aga gaa cag ctt cgc act			1037
Arg Pro Val Arg Pro Gln Ile Arg Leu Glu Arg Glu Gln Leu Arg Thr			
285	290	295	
gga cct tca aac aca gag gtc atc cac aac tat ggc cat gga ggc tac			1085
Gly Pro Ser Asn Thr Glu Val Ile His Asn Tyr Gly His Gly Gly Tyr			
300	305	310	
ggg ctc acc atc cac tgg gga tgt gcc ctg gag gca gcc aag ctc ttt			1133
Gly Leu Thr Ile His Trp Gly Cys Ala Leu Glu Ala Ala Lys Leu Phe			
315	320	325	330
ggg aga atc ctg gaa gaa aag aaa ttg tcc aga atg cca cca tcc cac			1181

Gly Arg Ile Leu Glu Glu Lys Leu Ser Arg Met Pro Pro Ser His  
 335 340 345  
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 Leu  
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 agttgtacta aatattaaa gtttctgaaa agtctqcaq caaagacaac tatctgtatgt 1594  
 tggtttaaccc agtgcgttgc aacctatct ggctatggaa ctctttgcc cagagcaccc 1654  
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 gacacccctgt tcctccatgtc ataacaacaa ctacagctt gattgaacaa gagactgagt 240  
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 Leu Ser Thr Ala Ile Cys Ile His Glu Arg Tyr His Ser Val Leu Gln  
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 cca ctg gac ata aag gtc tac gac gac cgc ttc acc cca ctc acc acc 1287  
 Pro Leu Asp Ile Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr  
 30 35 40

acc gac gtg gct gcc ggc ctc tgg cag ccc tac ctt tct gac ccc aac	1335
Thr Asp Val Ala Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn	
45 50 55 60	
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Asn Pro Gln Glu Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu	
65 70 75	
agc cat gtc cat tct ccc aac gct gaa aac ctg ggc ctg ttc cta atc	1431
Ser His Val His Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile	
80 85 90	
tcc ggc tac aac ctc ttc cat gaa gcc att ccc gac ccc tcc tgg aag	1479
Ser Gly Tyr Asn Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp Lys	
95 100 105	
gac aca gtt ctg gga ttt cgg aag ctg acc ccc aca gag ctg gat atg	1527
Asp Thr Val Leu Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp Met	
110 115 120	
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Phe Pro Asp Tyr Gly Tyr Trp Phe His Thr Ser Leu Ile Leu Glu	
125 130 135 140	
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Gly Lys Asn Tyr Leu Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg Gly	
145 150 155	
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Val Lys Phe Phe Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala Arg	
160 165 170	
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Glu Gly Ala Asp Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly Ala	
175 180 185	
cta cca cga gac ccc ctg ctg cag cca ggc cgg ggg cag atc atg aag	1767
Leu Gln Arg Asp Pro Leu Leu Gln Pro Gly Arg Gly Gln Ile Met Lys	
190 195 200	
gac cca gac agt tac tct tgg agg cat ctt cca gtt ggg aaa ctg gag	1815
Asp Pro Asp Ser Tyr Ser Trp Arg His Leu Pro Val Gly Lys Leu Glu	
205 210 215 220	
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gttttgtact tccggctgtc gca atg cgt gtg qtq qtq att gga gca gga gtc 173  
Met Arg Val Val Val Ile Gly Ala Gly Val  
1 5 10  
atc ggg ctg tcc acc gcc ctc tgc atc cat gag cgc tac cac tca gtc 221  
Ile Gly Leu Ser Thr Ala Leu Cys Ile His Glu Arg Tyr His Ser Val  
15 20 25  
ctg cag cca ctg gac ata aag gtc tac gcg gac cgc ttc acc cca ctc 269  
Leu Gln Pro Leu Asp Ile Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu  
30 35 40  
acc acc acc gac gtg gct gcc ggc ctc tgg cag ccc tac ctt tct gac 317  
Thr Thr Asp Val Ala Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp  
45 50 55  
ccc aac aac cca cag gag gcg acc ctt cct gga agg aca cag ttc tgg 365  
Pro Asn Asn Pro Gln Glu Ala Thr Leu Pro Gly Arg Thr Gln Phe Trp  
60 65 70  
gat ttc gga agc tgacccccc agagctggat atgttccccc attacggcta 417  
Asp Phe Gly Ser  
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245	250	255	
ctg gag gca ggc aag ctc ttt ggg aga atc ctg gaa gaa aag aaa ttg			932
Leu Glu Ala Ala Lys Leu Phe Gly Arg Ile Leu Glu Glu Lys Lys Leu			
260	265	270	
tcc aga atg cca cca tcc cac ctc tgaagactcc agtgactgtct gctcccccc			986
Ser Arg Met Pro Pro Ser His Leu			
275	280		
acaagaactc cttctccccc tcagccatg aatcaatgtg ctccatata agccattgt			1046
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tgggtctggc attataaaaga acagctgagg ctgtcattcc atgagtctt: agaagaaagg			1226
acagctcaga aaatcaaaga gcccaactgc ccagagccac agaaaatgaa ggataattga			1286
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Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Asp Val Ala			
35	40	45	
Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu			
50	55	60	
Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His			
65	70	75	80
Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn			
85	90	95	
Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp Lys Asp Thr Val Leu			
100	105	110	
Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp Met Phe Pro Asp Tyr			
115	120	125	
Gly Tyr Gly Trp Phe His Thr Ser Leu Ile Leu Glu Gly Lys Asn Tyr			
130	135	140	
Ile Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg Gly Val Lys Phe Phe			
145	150	155	160
Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala Arg Glu Gly Ala Asp			
165	170	175	
Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp			
180	185	190	
Pro Leu Leu Gln Pro Gly Arg Gly Gln Ile Met Lys Val Asp Ala Pro			
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Trp Met Lys His Phe Ile Leu Thr His Asp Pro Glu Arg Gly Ile Tyr			
210	215	220	
Asn Ser Pro Tyr Ile Ile Pro Gly Thr Gln Thr Val Thr Leu Gly Gly			
225	230	235	240
Ile Phe Gln Leu Gly Asn Trp Ser Glu Leu Asn Asn Ile Gln Asp His			
245	250	255	
Asn Thr Ile Trp Glu Gly Cys Cys Arg Leu Glu Pro Thr Leu Lys Asn			
260	265	270	
Ala Arg Ile Ile Gly Glu Arg Thr Gly Phe Arg Pro Val Arg Pro Gln			
275	280	285	

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 Val Ile His Asn Tyr Gly His Gly Tyr Gly Leu Thr Ile His Trp  
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 35 40 45  
 Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu  
 50 55 60  
 Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His  
 65 70 75 80  
 Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn  
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 Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp Lys Asp Thr Val Leu  
 100 105 110  
 Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp Met Phe Pro Asp Tyr  
 115 120 125  
 Gly Tyr Gly Trp Phe His Thr Ser Leu Ile Leu Glu Gly Lys Asn Tyr  
 130 135 140  
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 145 150 155 160  
 Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala Arg Glu Gly Ala Asp  
 165 170 175  
 Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp  
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Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Asp Val Ala  
35 40 45  
Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu  
50 55 60  
Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His  
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Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn  
85 90 95  
Leu Phe His Glu Ala Ile Pro Val Ala Arg Glu Gly Ala Asp Val Ile  
100 105 110  
Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp Pro Leu  
115 120 125  
Leu Gln Pro Gly Arg Gly Gln Ile Met Lys Val Asp Ala Pro Trp Met  
130 135 140  
Lys His Phe Ile Leu Thr His Asp Pro Glu Arg Gly Ile Tyr Asn Ser  
145 150 155 160  
Pro Tyr Ile Ile Pro Gly Thr Gln Thr Val Thr Leu Gly Gly Ile Phe  
165 170 175  
Gln Leu Gly Asn Trp Ser Glu Leu Asn Asn Ile Gln Asp His Asn Thr  
180 185 190  
Ile Trp Glu Gly Cys Cys Arg Leu Glu Pro Thr Leu Lys Asn Ala Arg  
195 200 205  
Ile Ile Gly Glu Arg Thr Gly Phe Arg Pro Val Arg Pro Gln Ile Arg  
210 215 220  
Leu Glu Arg Glu Gln Leu Arg Thr Gly Pro Ser Asn Thr Glu Val Ile  
225 230 235 240  
His Asn Tyr Gly His Gly Gly Tyr Gly Leu Thr Ile His Trp Gly Cys  
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<223> 8-132-179 : polymorphic base A or T

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<223> Xaa=Ser or Tyr

<220>  
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<222> 135  
<223> Xaa=Lys or Arg

<220>  
<221> VARIANT  
<222> 194  
<223> Xaa=Glu or Stop

<220>  
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<223> Xaa=Gly or Arg

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<223> Xaa=Ala or Asp

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Met Leu Glu		
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aaag ctg atg ggt gct gat tmt ctc cag ctt ttc aga tcc aga tat aca		103
Lys Leu Met Gly Ala Asp Xaa Leu Gln Leu Phe Arg Ser Arg Tyr Thr		
5 10 15		
ttg ggt aaa atc tac ttc ata ggt ttt caa arg agc att ctt ctg agc		151
Leu Gly Lys Ile Tyr Phe Ile Gly Phe Gln Xaa Ser Ile Leu Leu Ser		
20 25 30 35		
aaa tct gaa aac tct cta aac tct att gca aag gag aca gaa kaa gga		199
Lys Ser Glu Asn Ser Leu Asn Ser Ile Ala Lys Glu Thr Glu Xaa Gly		
40 45 50		
aca gag acg gta aca agg aaa gaa rga tgg aag aga agg cat gag gac		247
Arg Glu Thr Val Thr Arg Lys Glu Xaa Trp Lys Arg Arg His Glu Asp		
55 60 65		
gdc tat ttg gaa atg gca cag agg cat tta cag aga tca tta tgt cct		295
Gly Tyr Leu Glu Met Ala Gln Arg His Leu Gln Arg Ser Leu Cys Pro		
70 75 80		
tgg gtc tct tac ctt cct cag ccc tat gca gag ctt gaa gaa gta agc		343
Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu Glu Val Ser		
85 90 95		
agc cat gtt gga aaa gtc ttc atg gca aga aac tat gag ttc ctt gmc		391
Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu Phe Leu Xaa		
100 105 110 115		
tat gag gcc tct aar gac cgc agg cag cct cta gaa cga atg tgg acc		439
Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg Met Trp Thr		
120 125 130		
tgc aac tac aac cag caa aaa gac cag tca tgc aac cac aag gaa ata		487
Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His Lys Glu Ile		
135 140 145		
act tct acc aaa gct gaa tgagtttgc agcagattct tcccagccaa		535
Thr Ser Thr Lys Ala Glu		
150		
tccttctgat gacaatgttag tctggccaac atcttcactg gamtctgacg gactctgtgt		595
ctgggaccct gctgataaca cgtggatgtg ggattgtatt tgcaaytctc tggcgttacaa		655
gtgataaaat gccatttcta tgcacccacc tggcgtgt gactgggaga atytctctt		715
ttattaaawtg tgcttcaagt tttaaca		742

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<2><3> Xaa=Gly or Arg

<1><0>

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<1><0> 115

<2><3> Xaa=Ala or Asp

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<2><2> 53..64

<2><3> basic protease cleavage site

<2><0>

<2><1> SITE

<2><2> 122..123

<2><3> basic protease cleavage site

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<2><2> 132..142

<2><0>

<2><1> PEPTIDE

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<2><0>

<2><1> PEPTIDE

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Arg Tyr Thr Leu Gly Lys Ile Tyr Phe Ile Gly Phe Gln Xaa Ser Ile  
20 25 30  
Leu Leu Ser Lys Ser Glu Asn Ser Leu Asn Ser Ile Ala Lys Glu Thr  
35 40 45  
Glu Xaa Gly Arg Glu Thr Val Thr Arg Lys Glu Xaa Trp Lys Arg Arg  
50 55 60  
His Glu Asp Gly Tyr Leu Glu Met Ala Gln Arg His Leu Gln Arg Ser  
65 70 75 80  
Leu Cys Pro Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu  
85 90 95  
Glu Val Ser Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu  
100 105 110  
Phe Leu Xaa Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg  
115 120 125  
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Lys Glu Ile Thr Ser Thr Lys Ala Glu  
145 150

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tta tgt ctc tgg gtc tct tac ctt cct cag ccc tat gca gag ctt gaa 95  
Leu Cys Pro Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu  
20 25 30  
gaa gta agc agc cat gtt gga aaa gtc ttc atg gca aga aac tat gag 144  
Glu Val Ser Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu  
35 40 45  
ttc ctt gcc tat gag gcc tct aag gac cgc agg cag ctc cta gaa cga 192  
Phe Leu Ala Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg  
50 55 60  
atg tgg acc tgc aac tac aac cag caa aaa gac cag tca tgc aac cac 240  
Met Trp Thr Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His  
65 70 75 80  
aag gaa ata act tct acc aaa gct gaa tgatgttggaa agcagattct 287  
Lys Glu Ile Thr Ser Thr Lys Ala Glu  
85  
tcggcggccaa tcctttctgat gacaatgtat tctggccaaac atcttcactg gactctgacg 347  
gactctgtgt ctgggaccca gctgataaca cgtgtgtatg ggattgtatt tgcaactctc 407  
tggtcagtaa gtgataaaat gccatttcta tgcacccacc tggcctgtgt gactgggaga 467  
atctctttt 476

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<311> 89  
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20 25 30  
Glu Val Ser Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu  
35 40 45  
Phe Leu Ala Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg  
50 55 60  
Met Trp Thr Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His  
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Lys Glu Ile Thr Ser Thr Lys Ala Glu  
85

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<311> 1633  
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tgggtgcacg tggaaaggccgg acagagggtt gggaaacaaga cgttccagaa tcaggagttt 120  
cccttcagga aatagccatcc tgggtccccc cactgcgttt gtgtggcttc tccagcgttt 180  
tggtaacttcc ggctgctgca atg cgt gtg gtg att gga gca gga gtc atc 233  
Met Arg Val Val Val Ile Gly Ala Gly Val Ile  
1 5 10

ggg ctg tcc acc gcc ctc tgc atc cat gag cgc tac cac tca gtc ctg	281
Gly Leu Ser Thr Ala Leu Cys Ile His Glu Arg Tyr His Ser Val Leu	
15 20 25	
cag cca ctg cac ata aag gtc tac gcg gac cgc ttc acc cca ctc acc	329
Gln Pro Leu His Ile Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr	
30 35 40	
acc acc gac gtg gct ggc gtc tgg cag ccc ttc ctt gag ccc	377
Thr Thr Asp Val Ala Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro	
45 50 55	
aac aac cca cag gag ggc gac tgg aac cag acc ttt gac tat ctc	425
Asn Asn Pro Gln Glu Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu	
60 65 70 75	
ctg aac cat gtc cat tct ccc aac gct gaa aac ctg ggc ctg ttc cta	473
Leu Ser His Val His Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu	
80 85 90	
atc tcc ggc tac aac ctc ttc cat gaa gcc att ccc gac cct tcc tgg	521
Ile Ser Gly Tyr Asn Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp	
95 100 105	
aag gac aca gtt ctg gga ttt cgg aag ctg acc ccc aga gag ctg gat	569
Lys Asp Thr Val Leu Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp	
110 115 120	
atg ttc cca gat tac ggc tat ggc tgg ttc cac aca agc cta att ctg	617
Met Phe Pro Asp Tyr Gly Tyr Trp Phe His Thr Ser Leu Ile Leu	
125 130 135	
gag gga aag aac tat cta cag tgg ctg act gaa agg tta act gag agg	665
Glu Gly Lys Asn Tyr Leu Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg	
140 145 150 155	
gga gtg aag ttc ttc cag cgg aaa gtg gag tct ttt gag gag gtg gca	713
Gly Val Lys Phe Phe Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala	
160 165 170	
aga gaa ggc gca gac gtg att gtc aac tgc act ggg gta tgg gct ggg	761
Arg Glu Gly Ala Asp Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly	
175 180 185	
gcg cta caa cga gac ccc ctg cag cca ggc cgg ggg cag atc atg	809
Ala Leu Gln Arg Asp Pro Leu Leu Gln Pro Gly Arg Gly Gln Ile Met	
190 195 200	
aag gtg gac gcc cct tgg atg aag cac ttc att ctc acc cat gac cca	857
Lys Val Asp Ala Pro Trp Met Lys His Phe Ile Leu Thr His Asp Pro	
205 210 215	
gag aga ggc atc tac aat tcc ccg tac atc atc cca ggg acc cag aca	905
Glu Arg Gly Ile Tyr Asn Ser Pro Tyr Ile Ile Pro Gly Thr Gln Thr	
220 225 230 235	
gtt act ctt gga ggc atc ttc cag ttg gga aac tgg agt gaa cta aac	953
Val Thr Leu Gly Ile Phe Gln Leu Gly Asn Trp Ser Glu Leu Asn	
240 245 250	
aat atc cag gac cac aac acc att tgg gaa ggc tgc tgc aga ctg gag	1001
Asn Ile Gln Asp His Asn Thr Ile Trp Glu Gly Cys Cys Arg Leu Glu	
255 260 265	
ccc aca ctg aag aat gca aga att att ggt gaa gca act ggc ttc cgg	1049
Pro Thr Leu Lys Asn Ala Arg Ile Ile Gly Glu Ala Thr Gly Phe Arg	
270 275 280	
cca gta cgc ccc cag att cgg cta gaa aga gaa cag ctt cgc act gga	1097
Pro Val Arg Pro Gln Ile Arg Leu Glu Arg Glu Gln Leu Arg Thr Gly	
285 290 295	
cct tca aac aca gag gtc atc cac aac tat ggc cat gga ggc tac ggg	1145
Pro Ser Asn Thr Glu Val Ile His Asn Tyr Gly His Gly Gly Tyr Gly	
300 305 310 315	
ctc acc atc cac tgg gga tgt gcc ctg gag gca gcc aag ctc ttt ggg	1193
Leu Thr Ile His Trp Gly Cys Ala Leu Glu Ala Ala Lys Leu Phe Gly	

320	325	330	
aga atc ctg gaa gaa aag aaa ttg tcc aga atg cca cca tcc cac ctc			1241
Arg Ile Leu Glu Glu Lys Lys Leu Ser Arg Met Pro Pro Ser His Leu			
335	340	345	
tgaaagactcc agtgactgtc gcttcctccca adaagaatcc ctttctccca tcagccatgc			1301
atcaatgtt ctccttcata agccattgtt ttccttcac tttttcctt aaagaagcat			1361
gggttggatg aaagccatca agtcaatgtcc tggagaaggg ttcagccaa catggggccc			1421
cttcatcac tggatccat cttatccatc tgggtctggc attataaaaga acagstgagg			1481
ctgtcattcc atgatgttcc agaagaaaagg acatgtcaga aagtcaaaga ggcactgc			1541
ccaaqccac aqaaaatqqa qgataatttga qgtaagtaa cttgattaca agttgtacta			1601
acatattaaa gttctgaaa agtctgtcaa aa			1633
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Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Asp Val Ala			
35	40	45	
Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu			
50	55	60	
Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His			
65	70	75	80
Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn			
85	90	95	
Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp Lys Asp Thr Val Leu			
100	105	110	
Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp Met Phe Pro Asp Tyr			
115	120	125	
Gly Tyr Gly Trp Phe His Thr Ser Leu Ile Leu Glu Gly Lys Asn Tyr			
130	135	140	
Leu Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg Gly Val Lys Phe Phe			
145	150	155	160
Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala Arg Glu Gly Ala Asp			
165	170	175	
Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp			
180	185	190	
Pro Leu Leu Gln Pro Gly Arg Gly Gln Ile Met Lys Val Asp Ala Pro			
195	200	205	
Trp Met Lys His Phe Ile Leu Thr His Asp Pro Glu Arg Gly Ile Tyr			
210	215	220	
Asn Ser Pro Tyr Ile Ile Pro Gly Thr Gln Thr Val Thr Leu Gly Gly			
225	230	235	240
Ile Phe Gln Leu Gly Asn Trp Ser Glu Leu Asn Asn Ile Gln Asp His			
245	250	255	
Asn Thr Ile Trp Glu Gly Cys Cys Arg Leu Glu Pro Thr Leu Lys Asn			
260	265	270	
Ala Arg Ile Ile Gly Glu Ala Thr Gly Phe Arg Pro Val Arg Pro Gln			
275	280	285	
Ile Arg Leu Glu Arg Glu Gln Leu Arg Thr Gly Pro Ser Asn Thr Glu			
290	295	300	
Val Ile His Asn Tyr Gly His Gly Gly Tyr Gly Leu Thr Ile His Trp			
305	310	315	320
Gly Cys Ala Leu Glu Ala Ala Lys Leu Phe Gly Arg Ile Leu Glu Glu			

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tcc acg gct gtg tgc atc tcc aaa ctg gtg ccc cga tgc tcc gtt acc		96
Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr		
20 25 30		
atc att tca gac aag ttt act cca gat acc acc agt gat gtg gca gcc		144
Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala		
35 40 45		
gga atg ctt att cct cac act tat cca gat aca ccc att cac acg cag		190
Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln		
50 55 60		
aag cag tgg ttc aga gaa acc ttt aat cac ctc ttt gca att gcc aat		240
Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn		
65 70 75 80		
tct gca gaa gct gga gat gct ggt gtt cat ttg gta tca ggt tgg cag		288
Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Trp Gln		
85 90 95		
ata ttt cag agc act ccc act gaa gaa gtg cca ttc tgg gct gac gtg		336
Ile Phe Gln Ser Thr Pro Thr Glu Glu Val Pro Phe Trp Ala Asp Val		
100 105 110		
gtt ctg gga ttt cga aag atg act gag gct gag ctg aag aaa ttc ccc		384
Val Leu Gly Phe Arg Lys Met Thr Glu Ala Glu Leu Lys Lys Phe Pro		
115 120 125		
cag tat gtg ttt ggt cag gct ttt aca acc ctg aaa tgt gaa tgc cct		432
Gln Tyr Val Phe Gly Gln Ala Phe Thr Thr Leu Lys Cys Glu Cys Pro		
130 135 140		
gcc tac ctc ccc tgg ttg gag aaa agg ata aag gga agt gga ggc tgg		480
Ala Tyr Leu Pro Trp Leu Glu Lys Arg Ile Lys Gly Ser Gly Trp		
145 150 155 160		
aca ctc act ccc cga ata gaa gac ctg tgg gaa ctt cat ccc tcc ttt		528
Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu Leu His Pro Ser Phe		
165 170 175		
gac atc gtg gtc aac tgt tca ggc ctt gga agc aga cag ctt gca gga		576
Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser Arg Gln Leu Ala Gly		
180 185 190		
gac tca aag att ttc ccc gta agg ggc caa gtc ctc caa gtt cag gct		624
Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val Leu Gln Val Gln Ala		
195 200 205		
ccc tgg gtg gag cat ttt atc cga gat ggc agt ggg ctg aca tat att		672
Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser Gly Leu Thr Tyr Ile		
210 215 220		
tat ccc ggt aca tcc cat gta acc cta ggt gga act agg caa aaa ggg		720
Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly Thr Arg Gln Lys Gly		
225 230 235 240		
gac tgg aat ctg tcc ccc gat gca gaa aat agc aga gag att ctt tcc		768
Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser Arg Glu Ile Leu Ser		
245 250 255		
cga tgc tgt gct ctg gag ccc tcc ctc cac gga gcc tgc aac atc agg		816

Arg	Cys	Cys	Ala	Leu	Glu	Pro	Ser	Leu	His	Gly	Ala	Cys	Asn	Ile	Arg	
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gag	aag	gtg	ggc	ttg	agg	ccc	tac	agg	cca	ggc	gtg	cga	ctg	cag	aca	864
Glu	Lys	Val	Gly	Leu	Arg	Pro	Tyr	Arg	Pro	Gly	Val	Arg	Leu	Gln	Thr	
275				280								285				
gag	ctc	ttt	ggc	cga	gtt	gga	cag	agg	ctg	cct	gtt	gtc	cac	cac	tat	912
Glu	Leu	Leu	Ala	Arg	Asp	Gly	Gln	Arg	Leu	Pro	Val	Val	His	His	Tyr	
290				295							300					
ggc	cac	ggg	agt	ggg	ggc	atc	tca	gtg	cac	tgg	ggc	act	gtt	ctg	gag	960
Gly	His	Gly	Ser	Gly	Gly	Ile	Ser	Val	His	Trp	Gly	Thr	Ala	Leu	Glu	
305				310						315			320			
gcc	gcc	agg	ctg	gtg	agg	gtt	tgt	gtc	cat	gcc	ctc	agg	acc	ccc	att	1008
Ala	Ala	Arg	Leu	Val	Ser	Glu	Cys	Val	His	Ala	Leu	Arg	Thr	Pro	Ile	
325				330						335						
ccc	aag	tca	aac	ctg	tagatgacat	aaaatgacag	aaaaagagact	gagagactgt								1063
Pro	Lys	Ser	Asn	Leu												
340																
tgtatcaaagg	acagaacagg	ttcaaataac	ttttccactg	catgaaaagtt	taatttagaca											1123
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Met	Asp	Thr	Ala	Arg	Ile	Ala	Val	Val	Gly	Ala	Gly	Val	Val	Gly	Leu	
1				5				10				15				
tcc	acg	gt	gt	tgc	atc	tcc	aaa	ctg	gt	cc	cga	tgc	tcc	gtt	acc	96
Ser	Thr	Ala	Val	Cys	Ile	Ser	Lys	Leu	Val	Pro	Arg	Cys	Ser	Val	Thr	
20				25						30						
atc	att	tca	gac	aag	ttt	act	cca	gat	acc	acc	agt	gt	gca	gcc		144
Ile	Ile	Ser	Asp	Lys	Phe	Thr	Pro	Asp	Thr	Thr	Ser	Asp	Val	Ala	Ala	
35				40						45						
gga	atg	ctt	att	cct	cac	act	tat	cca	gat	aca	ccc	att	cac	acg	cag	192
Gly	Met	Leu	Ile	Pro	His	Thr	Tyr	Pro	Asp	Thr	Pro	Ile	His	Thr	Gln	
50				55						60						
aag	cag	tgg	tcc	aga	gaa	acc	ttt	aat	cac	ctc	ttt	gca	att	gcc	aat	240
Lys	Gln	Trp	Phe	Arg	Glu	Thr	Phe	Asn	His	Leu	Phe	Ala	Ile	Ala	Asn	
65				70						75			80			
tct	gca	gaa	gt	gat	gt	gt	cat	ttg	gt	tca	gg	ata	aag		288	
Ser	Ala	Glu	Ala	Gly	Asp	Ala	Gly	Val	His	Leu	Val	Ser	Gly	Ile	Lys	
85				90						95						
gga	agt	gga	ggc	tgg	aca	ctc	act	cg	cga	ata	gaa	gac	ctg	tgg	gaa	336
Gly	Ser	Gly	Gly	Trp	Thr	Leu	Thr	Arg	Arg	Ile	Glu	Asp	Leu	Trp	Glu	
100				105						110						
ctt	cat	ccg	tcc	ttt	gac	atc	gt	gtc	aat	tgt	tca	ggc	ctt	gga	agc	384
Leu	His	Pro	Ser	Phe	Asp	Ile	Val	Val	Asn	Cys	Ser	Gly	Leu	Gly	Ser	
115				120						125						
aga	cag	ctt	gca	gga	gac	tca	aag	att	tcc	cct	gt	agg	ggc	caa	gtc	432
Arg	Gln	Leu	Ala	Gly	Asp	Ser	Lys	Ile	Phe	Pro	Val	Arg	Gly	Gln	Val	
130				135						140						
ctc	caa	gtt	cag	gt	ccc	tgg	tgg	gag	cat	ttt	atc	cga	gat	ggc	agt	480
Leu	Gln	Val	Gln	Ala	Pro	Trp	Val	Glu	His	Phe	Ile	Arg	Asp	Gly	Ser	
145				150						155			160			
ggg	ctg	aca	tat	att	tat	cct	gg	aca	tca	cat	gt	acc	ct	gg	gga	528
Gly	Leu	Thr	Tyr	Ile	Tyr	Pro	Gly	Thr	Ser	His	Val	Thr	Leu	Gly	Gly	

165	170	175	
act agg caa aaa ggg gac tgg aat ctg tcc ccg gat gca gaa aat aac			576
Thr Arg Gln Lys Gly Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser			
180	185	190	
aga gag att ctt tcc cga tgc tgc gat ctg gag ccc tcc ctc cac gga			624
Arg Glu Ile Leu Ser Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly			
195	200	205	
gcc tgc aac atc agg gag aag gtc ttg agg ccc tcc agg cca ggc			672
Ala Cys Asn Ile Arg Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly			
210	215	220	
gtg cga ctg cag aca gag ctc ctt ggc gca gat gga gag agg ctg cct			720
Val Arg Leu Gln Thr Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro			
225	230	235	240
gtg cgt cac cac tat ggc cat ggg agt ggg ggc atc tca gtg cac tgg			768
Val Val His His Tyr Gly His Gly Ser Gly Ile Ser Val His Trp			
245	250	255	
ggc act gct ctg gag gcc ggc aac ctg gtc gtc gag tgc cat gca			816
Gly Thr Ala Leu Glu Ala Ala Arg Leu Val Ser Glu Cys Val His Ala			
260	265	270	
ctc agg acc ccc att ccc aag tca aac ctg tagatgacat aaaaatgacacag			866
Leu Arg Thr Pro Ile Pro Lys Ser Asn Leu			
275	280		
caaaagagact gagagactgt tgatcaaagg acagaacagg ttcaaataac tttttccactg			926
catgaaagg ttat tagaca ttctttgtt ttcaacatta gaagggtgt aacatgtaaag			986
ctgagcagg tagatgcct atagtcacag ctacttg			1023

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<311> 341

<312> PRT

<313> Homo sapiens

<400> 21

Met Asp Thr Ala Arg Ile Ala Val Val Gly Ala Gly Val Val Gly Leu			
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Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr			
20	25	30	
Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala			
35	40	45	
Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln			
50	55	60	
Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn			
65	70	75	80
Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Trp Gln			
85	90	95	
Ile Phe Gln Ser Thr Pro Thr Glu Glu Val Pro Phe Trp Ala Asp Val			
100	105	110	
Val Leu Gly Phe Arg Lys Met Thr Glu Ala Glu Leu Lys Lys Phe Pro			
115	120	125	
Gln Tyr Val Phe Gly Gln Ala Phe Thr Thr Leu Lys Cys Glu Cys Pro			
130	135	140	
Ala Tyr Leu Pro Trp Leu Glu Lys Arg Ile Lys Gly Ser Gly Gly Trp			
145	150	155	160
Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu Leu His Pro Ser Phe			
165	170	175	
Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser Arg Gln Leu Ala Gly			
180	185	190	
Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val Leu Gln Val Gln Ala			
195	200	205	
Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser Gly Leu Thr Tyr Ile			

210	215	220
Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly Thr Arg Gln Lys Gly		
225	230	235
Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser Arg Glu Ile Leu Ser		240
245	250	255
Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly Ala Cys Asn Ile Arg		
260	265	270
Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly Val Arg Leu Gln Thr		
275	280	285
Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro Val Val His His Tyr		
290	295	300
Gly His Gly Ser Gly Gly Ile Ser Val His Trp Gly Thr Ala Leu Glu		
305	310	315
Ala Ala Arg Leu Val Ser Glu Cys Val His Ala Leu Arg Thr Pro Ile		320
325	330	335
Pro Lys Ser Asn Leu		
340		

<210> 22

<211> 282

<212> PRT

<213> Homo sapiens

<400> 22

Met Asp Thr Ala Arg Ile Ala Val Val Gly Ala Gly Val Val Gly Leu		
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Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr		
20	25	30
Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala		
35	40	45
Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln		
50	55	60
Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn		
65	70	75
Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Ile Lys		
85	90	95
Gly Ser Gly Gly Trp Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu		
100	105	110
Leu His Pro Ser Phe Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser		
115	120	125
Arg Gln Leu Ala Gly Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val		
130	135	140
Leu Gln Val Gln Ala Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser		
145	150	155
Gly Leu Thr Tyr Ile Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly		
165	170	175
Thr Arg Gln Lys Gly Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser		
180	185	190
Arg Glu Ile Leu Ser Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly		
195	200	205
Ala Cys Asn Ile Arg Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly		
210	215	220
Val Arg Leu Gln Thr Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro		
225	230	235
Val Val His His Tyr Gly His Gly Ser Gly Gly Ile Ser Val His Trp		
245	250	255
Gly Thr Ala Leu Glu Ala Ala Arg Leu Val Ser Glu Cys Val His Ala		
260	265	270
Leu Arg Thr Pro Ile Pro Lys Ser Asn Leu		

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47

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<223> oligonucleotide 24-1461-256

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<221> allele

<222> 24

<223> polymorphic base A or G

<400> 26

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47